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L3             5 SEA FILE=HCAPLUS ABB=ON  L2 AND (?CANCER? OR ?CELL?(W)?PROLIF?
                 OR ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR? OR ?CARCIN? OR ?ANGIOGENES
                 IS? OR ?RETIN?(W)?ANGIOGENESIS? OR ?ARTHRITIS?)

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L3   ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:269873  HCAPLUS
DOCUMENT NUMBER:          140:297473
TITLE:                    Methods for inhibition of angiogenesis using
                          αvβ3 integrin antagonists
INVENTOR(S):              Brooks, Peter C.; Cheresh, David A.
PATENT ASSIGNEE(S):       The Scripps Research Institute, USA
SOURCE:                   U.S. Pat. Appl. Publ., 88 pp., Cont.-in-part of U.S.
                          Pat. Appl. 2003 176,334.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   5
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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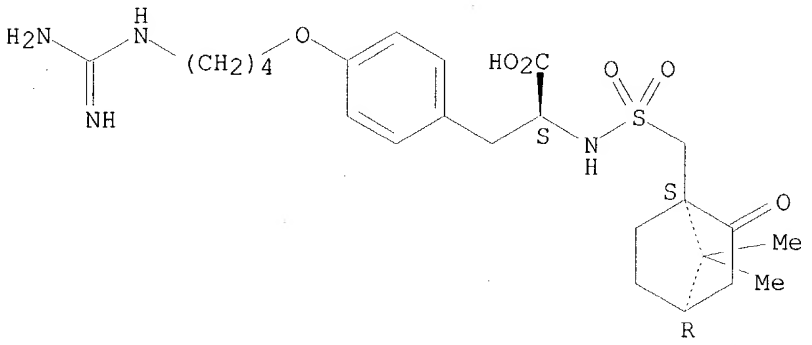
     US 2004063790      A1   20040401      US 2003-402212   20030328
     WO 9745137         A1   19971204      WO 1997-US9158   19970530
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US,
             UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
             ML, MR, NE, SN, TD, TG
     US 6500924         B1   20021231      US 1999-194468   19990323
     US 2003176334      A1   20030918      US 2002-115223   20020402
PRIORITY APPLN. INFO.:                  US 1996-15869P   P  19960531
                                        US 1996-18773P   P  19960531
                                        WO 1997-US9158   W  19970530
                                        US 1999-194468   A1 19990323
                                        US 2002-115223   A2 20020402
                                        US 1994-210715   A2 19940318
                                        US 1994-366665   A2 19941230
                                        US 1996-18733P   P  19960531
OTHER SOURCE(S):          MARPAT 140:297473
AB   The invention describes methods for inhibition angiogenesis in
     tissues using organic peptidomimetic αvβ3 antagonists, and
     particularly for inhibiting angiogenesis in inflamed tissues and
     in tumor tissues and metastases using therapeutic compns. containing
     αvβ3 antagonists.  The antagonists are organic compds. having a
     basic group and an acidic group spaced from one another by a distance in
     the range of about 10 Angstroms to about 100 Angstroms, as described in
     detail herein.
IT   199807-23-3P
     RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); RACT (Reactant or reagent); USES (Uses)
```

(methods for inhibition of **angiogenesis** using αvβ3 integrin antagonists)

RN 199807-23-3 HCAPLUS

CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-[[[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **188575-95-3P 188576-02-5P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

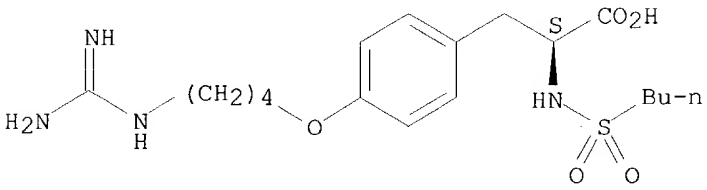
(methods for inhibition of **angiogenesis** using αvβ3 integrin antagonists)

Compound 7

RN 188575-95-3 HCAPLUS

CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

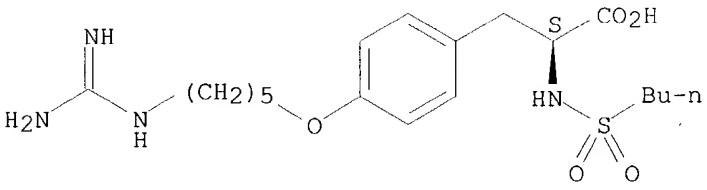
Absolute stereochemistry.



RN 188576-02-5 HCAPLUS

CN L-Tyrosine, O-[5-[(aminoiminomethyl)amino]pentyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:805756 HCAPLUS
DOCUMENT NUMBER: 128:48501
TITLE: Preparation of cyclopeptides, sulfonyltyrosine derivatives, and monoclonal antibodies as **antitumor** agents and αvβ5 mediated **angiogenesis** inhibitors for treatment of eye diseases
INVENTOR(S): Brooks, Peter; Cheresh, David A.; Friedlander, Martin
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Brooks, Peter; Cheresh, David A.; Friedlander, Martin
SOURCE: PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9745447	A1	19971204	WO 1997-US9099	19970530
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9732183	A1	19980105	AU 1997-32183	19970530
AU 738782	B2	20010927		
EP 907661	A1	19990414	EP 1997-927814	19970530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9709514	A	19990810	BR 1997-9514	19970530
CN 1226254	A	19990818	CN 1997-196818	19970530
CN 1226172	A	19990818	CN 1997-196822	19970530
JP 2002515036	T2	20020521	JP 1997-542914	19970530
RU 2195312	C2	20021227	RU 1998-123834	19970530
NO 9805575	A	19990201	NO 1998-5575	19981127
KR 2000016301	A	20000325	KR 1998-709874	19981130
KR 2000016302	A	20000325	KR 1998-709875	19981130

PRIORITY APPLN. INFO.: US 1996-15869P P 19960531
US 1996-18733P P 19960531
WO 1997-US9099 W 19970530

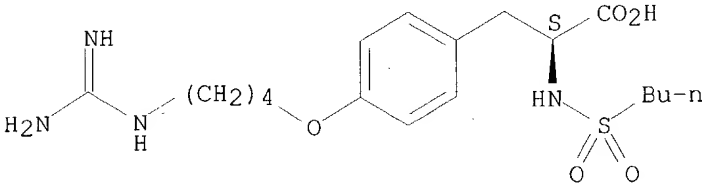
AB The present invention describes methods for inhibiting **angiogenesis** in tissues using vitronectin αvβ5 antagonists. The αvβ5-mediated **angiogenesis** is correlated with exposure to cytokines including vascular endothelial growth factor, transforming growth factor-α and epidermal growth factor. Inhibition of αvβ5-mediated **angiogenesis** is particularly preferred in vascular endothelial ocular neovascular diseases, in **tumor** growth and in inflammatory conditions, using therapeutic compns. containing αvβ5 antagonists. Thus, cyclopeptide cyclo(Arg-Asp-Gly-D-Phe-N-MeVal) (I) was prepared by standard solid-phase methods using 9-fluorenylmethoxycarbonyl (Fmoc) chemical I and related RGD cyclopeptides, as well as N-sulfonyl-O-guanidinylalkyltyrosine derivs., monoclonal antibodies, and synthetic matrix metalloproteins peptides and fusion proteins were tested for **angiogenesis** inhibition in a number of models, including an in vivo rabbit eye model.

IT **188575-95-3P 188576-02-5P 199807-23-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyltyrosine derivs. as αvβ5 mediated **angiogenesis** inhibitors for treatment of eye diseases)

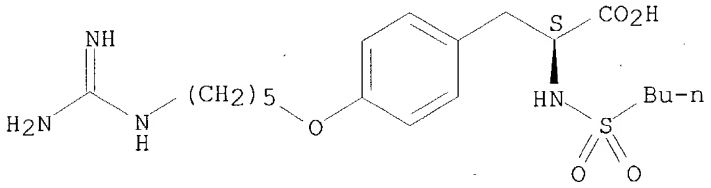
RN 188575-95-3 HCAPLUS
CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



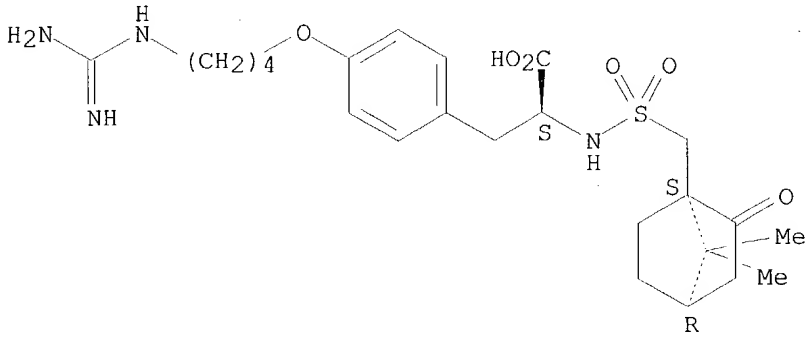
RN 188576-02-5 HCAPLUS
CN L-Tyrosine, O-[5-[(aminoiminomethyl)amino]pentyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 199807-23-3 HCAPLUS
CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-[[[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:803827 HCAPLUS
DOCUMENT NUMBER: 128:48497
TITLE: Preparation of cyclopeptides, fusion proteins,

monoclonal antibodies, and sulfonyltyrosine derivs. as αvβ5 mediated **angiogenesis** inhibitors and **antitumor** agents

INVENTOR(S): Brooks, Peter; Cheresh, David A.
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Brooks, Peter; Cheresh, David A.
SOURCE: PCT Int. Appl., 234 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9745137	A1	19971204	WO 1997-US9158	19970530
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9732893	A1	19980105	AU 1997-32893	19970530
AU 733303	B2	20010510		
CN 1226254	A	19990818	CN 1997-196818	19970530
CN 1226172	A	19990818	CN 1997-196822	19970530
EP 951295	A1	19991027	EP 1997-928698	19970530
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000516201	T2	20001205	JP 1997-542941	19970530
RU 2194528	C2	20021220	RU 1998-123833	19970530
NO 9805574	A	19990201	NO 1998-5574	19981127
KR 2000016301	A	20000325	KR 1998-709874	19981130
KR 2000016302	A	20000325	KR 1998-709875	19981130
US 6500924	B1	20021231	US 1999-194468	19990323
US 2003176334	A1	20030918	US 2002-115223	20020402
US 2004063790	A1	20040401	US 2003-402212	20030328

PRIORITY APPLN. INFO.:

US 1996-15869P	P	19960531
US 1996-18733P	P	19960531
US 1994-210715	A2	19940318
US 1994-366665	A2	19941230
US 1996-18773P	P	19960531
WO 1997-US9158	W	19970530
US 1999-194468	A1	19990323
US 2002-115223	A2	20020402

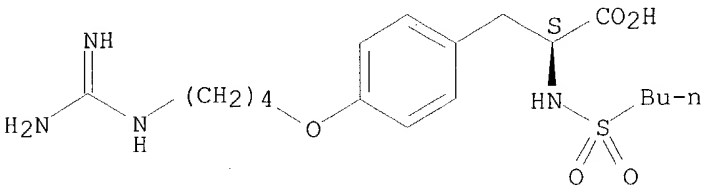
AB The present invention describes methods for inhibiting **angiogenesis** in tissues using vitronectin αvβ5 antagonists. The αvβ5-mediated **angiogenesis** is correlated with exposure to cytokines including vascular endothelial growth factor, transforming growth factor-α and epidermal growth factor. Inhibition of αvβ5-mediated **angiogenesis** is particularly preferred in vascular endothelial ocular neovascular diseases, in **tumor** growth and in inflammatory conditions, using therapeutic compns. containing αvβ5 antagonists. Thus, cyclopeptide cyclo(Arg-Asp-Gly-D-Phe-N-MeVal) (I) was prepared by standard solid-phase methods using 9-fluorenylmethoxycarbonyl (Fmoc) chemical I and related RGD cyclopeptides, as well as N-sulfonyl-O-guanidinylalkyltyrosine derivs., monoclonal antibodies, and synthetic matrix metalloproteins

peptides and fusion proteins were tested for **angiogenesis** inhibition in a number of **antitumor** models.

IT **188575-95-3P 188576-02-5P 199807-23-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of sulfonyltyrosine derivs. as αvβ5 mediated **angiogenesis** inhibitors and **antitumor** agents)

RN 188575-95-3 HCAPLUS
CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 188576-02-5 HCAPLUS
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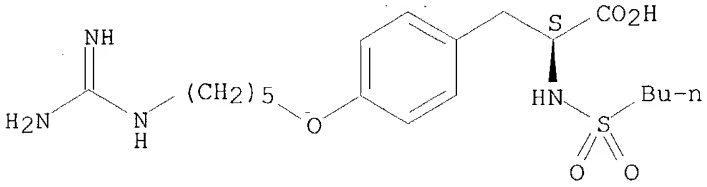
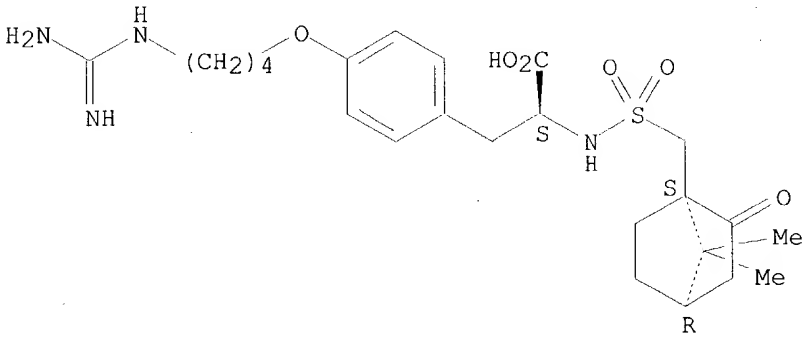
Absolute stereochemistry.



RN 199807-23-3 HCAPLUS
CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-[[[(1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]hept-1-yl]methyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:467800 HCAPLUS
DOCUMENT NUMBER: 127:95612
TITLE: Preparation of tyrosine-derivative αV-integrin inhibitors
INVENTOR(S): Diefenbach, Beate; Fittschen, Claus; Gante, Joachim; Goodman, Simon; Wiesner, Matthias; Rippmann, Friedrich
PATENT ASSIGNEE(S): Merck Patent Gmbh, Germany
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19548709	A1	19970703	DE 1995-19548709	19951223
CA 2241149	AA	19970703	CA 1996-2241149	19961216
WO 9723451	A1	19970703	WO 1996-EP5646	19961216
W: AU, BR, CA, CN, CZ, FI, HU, JP, KR, MX, NO, PL, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9713016	A1	19970717	AU 1997-13016	19961216
EP 879227	A1	19981125	EP 1996-944578	19961216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1205687	A	19990120	CN 1996-199305	19961216
BR 9612201	A	19990713	BR 1996-12201	19961216
JP 2000502664	T2	20000307	JP 1997-523282	19961216
ZA 9610725	A	19970626	ZA 1996-10725	19961219
NO 9802907	A	19980622	NO 1998-2907	19980622

PRIORITY APPLN. INFO.: DE 1995-19548709 A 19951223
WO 1996-EP5646 W 19961216

OTHER SOURCE(S): MARPAT 127:95612
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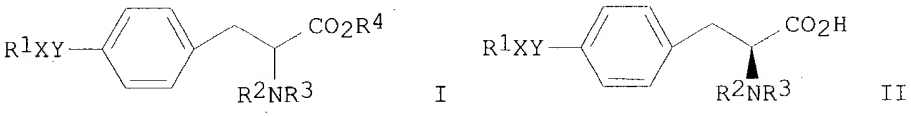
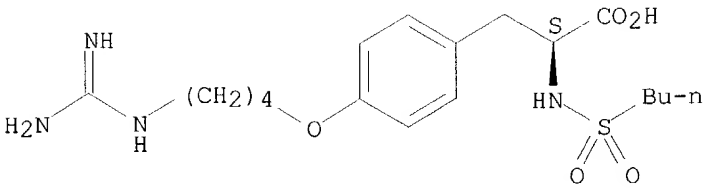


AB The title compds. [I; R1 = H, CN, N3, NH2, C(:NH), H2N(C:NH)NH; R2, R3 = H, A, ASO2, 10-(campheryl)SO2, CO2A, amino-blocking group, etc.; A, R4 = H, alkyl, PhCH2; X = alkylene, 1,4-piperidinyl; Y = O, CONH, C.tplbond.C], useful as αV-integrin inhibitors, are prepared and I-containing formulations presented. Thus, II [R1 = H2NC(:NH)NH, R2 = H, R3 = BuSO2, X = butylene, Y = O] was prepared and demonstrated a IC50 of 0.4 nM against the binding of vitronectin to the αVβ3 receptor.

IT **188575-95-3P 188576-02-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine-derivative αV-integrin inhibitors)

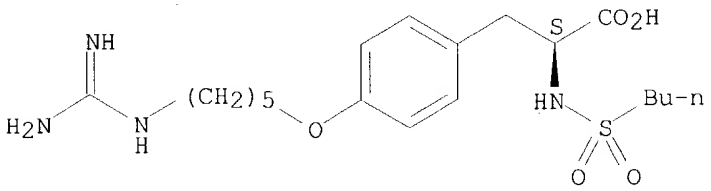
RN 188575-95-3 HCAPLUS
CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 188576-02-5 HCAPLUS
CN L-Tyrosine, O-[5-[(aminoiminomethyl)amino]pentyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

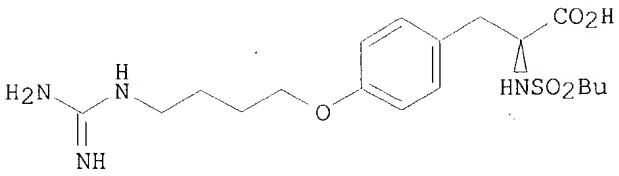


L3 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:265569 HCAPLUS
DOCUMENT NUMBER: 126:251416
TITLE: Preparation of tyrosine derivatives as compounds useful for inhibition of vitronectin αvβ5 integrin-mediated **angiogenesis**
INVENTOR(S): Brooks, Peter; Cheresh, David A.; Friedlander, Martin
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Brooks, Peter; Cheresh, David A.; Friedlander, Martin
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9706791	A1	19970227	WO 1996-US13194	19960813
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
AU 9668466	A1	19970312	AU 1996-68466	19960813
AU 726793	B2	20001123		
EP 844874	A1	19980603	EP 1996-928868	19960813
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1198667	A	19981111	CN 1996-197429	19960813
JP 11511171	T2	19990928	JP 1996-509460	19960813
RU 2214268	C2	20031020	RU 1998-104128	19960813
ZA 9606886	A	19970424	ZA 1996-6886	19960814

NO 9800622 A 19980407 NO 1998-622 19980213
PRIORITY APPLN. INFO.: US 1995-514799 A 19950814
WO 1996-US13194 W 19960813

GI



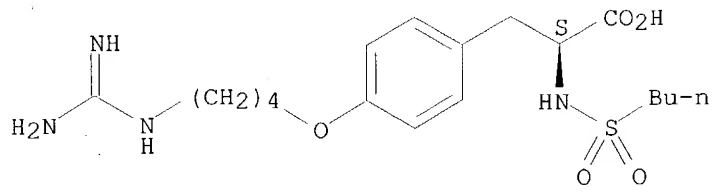
I

AB The present invention describes methods for inhibiting **angiogenesis** in tissues using vitronectin αvβ5 antagonists. The αvβ5-mediated **angiogenesis** is correlated with exposure to cytokines including vascular endothelial growth factor, transforming growth factor-α and epidermal growth factor. Inhibition of αvβ5-mediated **angiogenesis** is particularly preferred in vascular endothelial ocular neovascular diseases, in **tumor** growth and in inflammatory conditions, using therapeutic compns. containing αvβ5 antagonists. Thus, Boc-Tyr-OCH2Ph (preparation given) was converted in 6 steps into guanidino derivative I. I and related guanidine and amidine derivs. were useful as **angiogenesis** inhibitors.

IT **188575-95-3P 188576-02-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine derivs. as compds. useful for inhibition of vitronectin αvβ5 integrin-mediated **angiogenesis**)

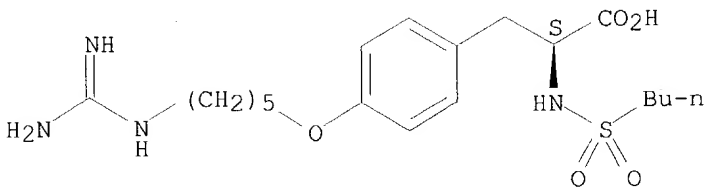
RN 188575-95-3 HCAPLUS
CN L-Tyrosine, O-[4-[(aminoiminomethyl)amino]butyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 188576-02-5 HCAPLUS
CN L-Tyrosine, O-[5-[(aminoiminomethyl)amino]pentyl]-N-(butylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his ful

FILE 'REGISTRY' ENTERED AT 11:24:08 ON 22 JUN 2004
L1 3 SEA ABB=ON (188575-95-3 OR 199807-23-3 OR 188576-02-5)/RN
compds 7 & 10* compd 12 compd 14

FILE 'HCAPLUS' ENTERED AT 11:26:16 ON 22 JUN 2004
L2 5 SEA ABB=ON L1
L3 5 SEA ABB=ON L2 AND (?CANCER? OR ?CELL?(W)?PROLIF? OR ?NEOPLASM? OR ?TUMOR? OR ?TUMOUR? OR ?CARCIN? OR ?ANGIOGENESIS? OR ?RETIN?(W)?ANGIOGENESIS? OR ?ARTHRITIS?) 5 hits in CA Plus - attached

FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 11:28:26 ON 22 JUN 2004
L4 0 SEA ABB=ON L3 0 hits in other databases

FILE 'REGISTRY' ENTERED AT 11:33:57 ON 22 JUN 2004
D SAVED
ACT HAR552L18/L

L5 STR

D QUE STAT L5
L6 0 SEA SSS SAM L5 0 hits for structure (compd 9)

FILE 'BEILSTEIN' ENTERED AT 11:47:22 ON 22 JUN 2004
L7 0 SEA SSS SAM L5 0 hits for structure (compd 9)

* These are stereoisomers which aren't usually distinguished for RN's

I could not locate compd. 9 in "Inventor's work" or by its exact structure. See L6 & L7.

Alana, please let me know if you'd like for me to go over this. Thanks, MJ